Potential predictive value of PIK3CA and ESR1 by liquid biopsy NGS for late-line hormone-based therapies in ER+/HER2-metastatic breast cancer (MBC)

Wei-Wu Chen, M.D.
Attending physician of Department of Oncology,
National Taiwan University Hospital
Taipei, Taiwan

With more endocrine therapies- (ET) based treatment (tx) available, genomic markers that could assist in the prediction of tx outcome is critical. We enrolled 163 ER+/HER2- MBC patients to test for circulating tumor DNA (ctDNA) with targeted NGS that includes regions of the ESR1 ligand-binding domain, PIK3CA hotspots, and TP53 DNA-binding domain mutations. The median level of recovered cfDNA was 38.5 ng (range 4.4-1935) and cfDNA level was significantly and inversely correlated with PFS (p = 0.0032). With ctDNA variant allelic frequency (VAF) at ≥ 0.5% as a threshold for positive calling, 100 (61.3%), 41 (25.1%), and 25 (15.3) pts have at least one ESR1, PIK3CA, and TP53 mutation, respectively. The median PFS of the cohort was 8.3 mos (95% CI 5.7 – 11.1 mos). PIK3CA MT in ctDNA was associated with worse outcome in all patients (HR 1.91, 95% CI 1.20 to 3.04, p = 0.0064) and the subgroups of ET + everolimus (HR 2.20, 95% CI 1.10 – 4.39, p = 0.025) and ET + metronomic chemotherapy (HR 5.34, 95% CI 1.63- 17.54, p = 0.006). The presence of TP53 MT ctDNA was also associated with worse PFS (HR 1.81, p = 0.043). Interestingly, for patients who have either PIK3CA or TP53 mutation, the presence of ESR1 mutation did not have a deteriorating prognostic impact. Using ctDNA targeted NGS panel, we demonstrated that PIK3CA and TP53 mutations exerted a stronger prognostic impact than ESR1 mutation in ER+/HER2- MBC.